

**Notice of Allowability**

Application No.

09/832,929

Examiner

Hope A. Robinson

Applicant(s)

ROSEN ET AL.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☐ This communication is responsive to 4/5/04.
2. ☒ The allowed claim(s) is/are 1-21 and 26-29.
3. ☒ The drawings filed on 30 November 2001 are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☐ All   b) ☐ Some\*   c) ☐ None   of the:
    1. ☐ Certified copies of the priority documents have been received.
    2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
  6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
    - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
    - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date \_\_\_\_\_
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date \_\_\_\_\_
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other \_\_\_\_\_

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### EXAMINER'S AMENDMENT

1. An Examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.
2. Authorization of this Examiner's amendment was given in a telephone interview with Mr. Mr. Charles Van Horn on March 26, 2004 and Yuko Soneoka for Mr. Charles Van Horn on May 14, 2004.
3. The claims have been amended as follows:  
Please cancel claims 22-25.

Claim 1 (Currently Amended) An albumin fusion protein comprising a member selected from the group consisting of :

(a) an antibody or antibody fragment that specifically binds human epidermal growth factor receptor-2 (HER2) and albumin, [comprising the amino acid sequence of SEQ ID NO:18] wherein albumin comprises the amino acid sequence of SEQ ID NO:18;

(b) an antibody or antibody fragment that specifically binds human epidermal growth factor receptor-2 (HER2) and a fragment [or variant] of the amino acid sequence of SEQ ID NO:18, wherein said fragment [or variant] of the amino acid sequence of SEQ ID NO:18 [has

albumin activity] has the ability to prolong the shelf-life of the antibody or antibody fragment that specifically binds HER2, compared to the shelf-life of the antibody or antibody fragment that specifically binds HER2, in an unfused state;

(c) [an antibody or antibody fragment that specifically binds HER2, and a fragment or a variant of the amino acid sequence of SEQ ID NO:18, wherein said fragment or variant of the amino acid sequence of SEQ ID NO:18 has albumin activity, and further wherein said albumin activity is the ability to prolong the shelf life of the antibody or antibody fragment that specifically binds HER2 compared to the shelf-life of the antibody or antibody fragment that specifically binds HER2 in an unfused state;] an antibody or antibody fragment that specifically binds human epidermal growth factor receptor-2 (HER2) and a fragment of the amino acid sequence of SEQ ID NO:18, wherein said fragment has the ability to prolong the shelf-life of the antibody or antibody fragment that specifically binds HER2 compared to the shelf-life of the antibody or antibody fragment that specifically binds HER2, in an unfused state, and further wherein the said fragment comprises amino acid residues 1-387 of SEQ ID NO:18;

(d) [an antibody fragment that specifically binds HER2, and a fragment or a variant of the amino acid sequence of SEQ ID NO:18, wherein said fragment or variant of the amino acid sequence of SEQ ID NO:18 has albumin activity, and further wherein the fragment or variant of the amino acid sequence of SEQ ID NO:18 comprises the amino acids 1-387 of SEQ ID NO:18;] a fragment of an antibody that specifically binds human epidermal growth factor receptor-2 (HER2) and albumin comprising the amino acid sequence of SEQ ID NO:18, wherein said fragment has a biological activity of the antibody that specifically binds HER2;

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(e) [an antibody or antibody fragment that specifically binds HER2, and albumin, or fragment or variant thereof, of (a) to (d) wherein the antibody or antibody fragment that specifically binds HER2, is fused to the N-terminus of albumin, or the N-terminus of the fragment or variant of albumin;] an antibody or antibody fragment that specifically binds human epidermal growth factor receptor-2 (HER2), and albumin, or fragment thereof, of (a) to (d), wherein the antibody or antibody fragment that specifically binds HER2, is fused to the N-terminus of albumin or the N-terminus of the fragment of albumin;

(f) [an antibody or antibody fragment that specifically binds HER2, and albumin, or fragment or variant thereof, of (a) to (d), wherein the antibody or antibody fragment that specifically binds HER2, is fused to the C-terminus of albumin, or the C-terminus of the fragment or variant of albumin;] an antibody or antibody fragment that specifically binds human epidermal growth factor receptor-2 (HER2), and albumin, or fragment thereof, of (a) to (d), wherein the antibody or antibody fragment that specifically binds HER2, is fused to the C-terminus of albumin, or the C-terminus of the fragment of albumin;

(g) [an antibody or antibody fragment that specifically binds HER2, and albumin, or fragment or variant thereof, of (a) to (d), wherein the antibody or antibody fragment that specifically binds HER2, is fused to the N-terminus and C-terminus of albumin, or the N-terminus and the C-terminus of the fragment or variant of albumin;] an antibody or antibody fragment that specifically binds human epidermal growth factor receptor-2 (HER2), and albumin or fragment thereof, of (a) to (d), wherein the an antibody or antibody fragment that specifically binds HER2, is fused to the N-terminus and C-terminus of albumin, or the N-terminus and the C-terminus of the fragment of albumin;

(h) [an antibody or antibody fragment that specifically binds HER2, and albumin, or fragment or variant thereof, of (a) to (g), wherein the antibody or antibody fragment that specifically binds HER2, is separated from the albumin or the fragment or variant of albumin by a linker and;] an antibody or antibody fragment that specifically binds human epidermal growth factor receptor-2 (HER2), and albumin or fragment thereof, of (a) to (g), wherein the an antibody or antibody fragment that specifically binds HER2, is separated from the albumin or the fragment of albumin by a linker; and

(i) an antibody or antibody fragment that specifically binds human epidermal growth factor receptor-2 (HER2) [HER2], and albumin or fragment [or variant] thereof, of (a) to (h), wherein the albumin fusion protein has the following formula:

R1-L-R2; R2-L-R1; or R1-L-R2-L-R1,

and further wherein R1 is an antibody or antibody fragment that specifically binds HER2, L is a peptide linker, and R2 is albumin comprising the amino acid sequence of SEQ ID NO:18 or a fragment [or variant] of albumin.

Claim 2 (Previously Presented) The albumin fusion protein of claim 1, wherein the shelf-life of the albumin fusion protein is greater than the shelf-life of the antibody or antibody fragment that specifically binds HER2, in an unfused state.

Claim 3 (Currently Amended) The albumin fusion protein of claim 1, wherein the in vitro biological activity of the antibody or antibody fragment that specifically binds HER2, fused to albumin, or fragment [or variant] thereof, is greater than the in vitro biological activity of the antibody or antibody fragment that specifically binds HER2, in an unfused state.

Claim 4 (Currently Amended) The albumin fusion protein of claim 1, wherein the in vivo biological activity of the antibody or antibody fragment that specifically binds HER2, fused to albumin, or fragment [or variant] thereof, is greater than the in vivo biological activity of the antibody or antibody fragment that specifically binds HER2, in an unfused state.

Claim 5 (Currently Amended) An albumin fusion protein comprising an antibody or antibody fragment that specifically binds HER2, inserted into an albumin, or fragment [or variant] thereof, comprising the amino acid sequence of SEQ ID NO:18 or fragment [or variant] thereof.

Claim 6 (Currently Amended) An albumin fusion protein comprising an antibody or antibody fragment that specifically binds human epidermal growth factor receptor-2 (HER2), [HER2,] inserted into an albumin, or fragment [or variant] thereof, comprising an amino acid sequence selected from the group consisting of:

- (a) amino acids residues 54 to 61 of SEQ ID NO:18;
- (b) amino acids residues 76 to 89 of SEQ ID NO:18;
- (c) amino acids residues 92 to 100 of SEQ ID NO:18;
- (d) amino acids residues 170 to 176 of SEQ ID NO:18;
- (e) amino acids residues 247 to 252 of SEQ ID NO:18;
- (f) amino acids residues 266 to 277 of SEQ ID NO:18;
- (g) amino acids residues 280 to 288 of SEQ ID NO:18;
- (h) amino acids residues 362 to 368 of SEQ ID NO:18;
- (i) amino acids residues 439 to 447 of SEQ ID NO:18;
- (j) amino acids residues 462 to 475 of SEQ ID NO:18;

- (k) amino acids residues 478 to 486 of SEQ ID NO:18; and
- (l) amino acids residues 560 to 566 of SEQ ID NO:18.

Claim 7 (Currently Amended) The albumin fusion protein of claim 5, wherein said albumin fusion protein comprises a [portion] fragment of albumin sufficient to prolong the shelf-life of the antibody or antibody fragment that specifically binds HER2, as compared to the shelf-life of the antibody or antibody fragment that specifically binds HER2, in an unfused state.

Claim 8 (Currently Amended) The albumin fusion protein of claim 6, wherein said albumin fusion protein comprises a [portion] fragment of albumin sufficient to prolong the shelf-life of the antibody or antibody fragment that specifically binds HER2, as compared to the shelf-life of the antibody or antibody fragment that specifically binds HER2, in an unfused state.

Claim 9 (Currently Amended) The albumin fusion protein of claim 5, wherein said albumin fusion protein comprises a [portion] fragment of albumin sufficient to prolong the in vitro biological activity of the antibody or antibody fragment that specifically binds HER2, fused to albumin as compared to the in vitro biological activity of the antibody or antibody fragment that specifically binds HER2, in an unfused state.

Claim 10 (Currently Amended) The albumin fusion protein of claim 6, wherein said albumin fusion protein comprises a [portion] fragment of albumin sufficient to prolong the in vitro biological activity of the antibody or antibody fragment that specifically binds HER2, fused to albumin as compared to the in vitro biological activity of the antibody or antibody fragment that specifically binds HER2, in an unfused state.

Claim 11 (Currently Amended) The albumin fusion protein of claim 5, wherein said albumin fusion protein comprises a [portion] fragment of albumin sufficient to prolong the in vivo biological activity of the antibody or antibody fragment that specifically binds HER2, fused to albumin as compared to the in vivo biological activity of the antibody or antibody fragment that specifically binds HER2, in an unfused state.

Claim 12 (Currently Amended) The albumin fusion protein of claim 6, wherein said albumin fusion protein comprises a [portion] fragment of albumin sufficient to prolong the in vivo biological activity of the antibody or antibody fragment that specifically binds HER2, fused to albumin as compared to the in vivo biological activity of the antibody or antibody fragment that specifically binds HER2, in an unfused state.

Claim 13 (Original) The albumin fusion protein of any one of claims 1-12, which is non-glycosylated.

Claim 14 (Original) The albumin fusion protein of any one of claims 1-12, which is expressed in yeast.

Claim 15 (Original) The albumin fusion protein of claim 14, wherein the yeast is glycosylation deficient.

Claim 16 (Original) The albumin fusion protein of claim 14, wherein the yeast is glycosylation and protease deficient.

Claim 17 (Original) The albumin fusion protein of any one of claims 1-12, which is expressed by a mammalian cell.

Claim 18 (Original) The albumin fusion protein of any one of claims 1-12, wherein the albumin fusion protein is expressed by a mammalian cell in culture.



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Claim 19 (Original) The albumin fusion protein of any one of claims 1-12, wherein the albumin fusion protein further comprises a secretion leader sequence.

Claim 20 (Original) A composition comprising the albumin fusion protein of any one of claims 1-12 and a pharmaceutically acceptable carrier.

Claim 21 (Original) A kit comprising the composition of claim 20.

Claim 26 (Presently Amended) A method of extending the shelf-life of [Therapeutic protein:X or fragment or variant thereof,] an antibody that specifically binds human epidermal growth factor receptor-2 (HER2) or fragment thereof, comprising the step of fusing the [Therapeutic protein:X, or fragment or variant thereof,] antibody that specifically binds HER2 or fragment thereof, to albumin or albumin fragment [or variant thereof], sufficient to extend the shelf-life of [Therapeutic protein:X or fragment or variant thereof,] the antibody that specifically binds HER2 or fragment thereof, compared to the shelf-life of the [Therapeutic protein:X, or fragment or variant thereof,] antibody that specifically binds HER2 or fragment thereof, in an unfused state.

Claim 27 (Original) A nucleic acid molecule comprising a polynucleotide sequence encoding the albumin fusion protein of any one of claims 1-12.

Claim 28 (Original) A vector comprising, the nucleic acid molecule of claim 27.

Claim 29 (Original) A host cell comprising the nucleic acid molecule of claim 28.

***Information Disclosure Statement***

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4. The Information Disclosure Statement filed April 5, 2004 has been considered. Page 3 of the IDS lists several applications and pre-grant publications which are pending or not yet in printed form, although reviewed have been lined through as these applications/publications cannot appear on the face of the patent.

5. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance".


### ***Conclusion***

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday from 9:00 a.m. to 6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S.F. Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson, MS 

Patent Examiner



KAREN COCHRANE CARLSON, PH.D  
PRIMARY EXAMINER